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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/856,371	05/21/2001	Hidetoshi Uemura	UEMURA 7	8300

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EXAMINER	
PAK, YONG D	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 10/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/856,371	UEMURA ET AL.	
	Examiner	Art Unit	
	Yong D Pak	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20-24,29,31-36 and 41-53* is/are pending in the application.

4a) Of the above claim(s) *20-24,29,31-35,42-46 and 48-53* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *36,41 and 47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/9/02 & 5/21/01*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed on July 20, 2004, canceling claims 25-28 and 30 and amending claim 41, has been entered.

This application is a 371 of PCT/JP99/06475.

Claims 20-24, 29, 31-36 and 41-53 are pending.

Election/Restrictions

Applicant's election with traverse of Group I with a further election of SEQ ID NO:10 in the reply filed on June 30, 2004 is acknowledged. The traversal is on the ground(s) that claim 36 of Group VII should be rejoined with Group I since claim 36 is drawn to a composition comprising the protein of Group I. This is found persuasive and claim 36 is now rejoined with Group I and claims 36, 41 an 47 are now examined together

The requirement is still deemed proper and is therefore made FINAL.

Claims 20-24, 29, 31-35, 42-46 and 48-53 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on June 30, 2004.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Information Disclosure Statement

The information disclosure statements (IDS) submitted on April 9, 2002 and May 21, 2001 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements are being considered by the examiner.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 41 and 47 are rejected under 35 U.S.C. 101 because the claimed invention is directed to a non-statutory subject matter.

Claims 41 and 47, as written, do not sufficiently distinguish over proteins as they exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. See Diamond v. Chakrabarty, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of "Isolated" or "Purified" as taught by the specification. See MPEP 2105.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 36, 41 and 47 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 36, 41 and 47 are drawn to a polypeptide with no limitations to its function. Therefore, the claims are drawn to a large variable genus of polypeptides having unknown activity or inactive variants. The specification does not describe the function of all the polypeptide sequences derived or modified from SEQ ID NO:10 and therefore, many functionally and structurally unrelated polynucleotides are encompassed within the scope of these claims. Therefore, applicants fail to describe representative species by identifying characteristics or functional characteristics other than being fragments/variants of SEQ ID NO:10.

The claims are also drawn to a polypeptide comprising SEQ ID NO:10 and fragments of SEQ ID NO:10 modified by deletion, addition, insertion, or substitution having serine protease activity, unknown activity or inactive variants. The single species of the serine protease human of SEQ ID NO: 10 is insufficient to describe the whole genus containing a vast number and combinations of amino acid deletions, insertions, additions, or substitutions. The specification fails to place limitations on the serine

protease structure or disclose which amino acid(s) of SEQ ID NO: 10 can be safely modified and still impart serine protease X activity. Therefore, the specification fails to describe other representative species from other sources or by identifying characteristics or structural properties or function.

Given this lack of description of the representative species encompassed by the genus of the claims, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the inventions of claims 36, 41 and 47.

Claim 36, 41 and 47 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polypeptide of SEQ ID NO:10, does not reasonably provide enablement for polypeptides having structure different from SEQ ID NO:10. The specification also does not reasonably provide enablement for polynucleotides encoding polynucleotide having unknown function. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in

the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The claims are drawn to polynucleotides encoding polypeptides having unknown function. The claims broadly encompass not only serine protease, but any fragments/variants of SEQ ID NO:10. The claims also encompass molecules having very low structural similarity to the serine protease of SEQ ID NO:10 and proteins of unknown functionality. Therefore, these claims encompass polypeptides having structures with low homology to SEQ ID NO:10. Therefore, the breadth of these claims is much larger than the scope enable by the specification.

The specification does teach how to make variants of SEQ ID NO:1. However, the function of a polypeptide cannot be predicted from its structure and the specification does not teach how to use polypeptides with unknown function. The quantity of experimentation in this area is extremely large since there is significant variability in the activity of the polynucleotides in the claims. It would require significant study to identify the actual function of the encoded polypeptides and identifying a use for the polypeptide would be an inventive, unpredictable and difficult undertaking. This would require years of inventive effort, with each of the many intervening steps, upon effective reduction to practice, not providing any guarantee of success in the succeeding steps.

The art is extremely unpredictable with regard to protein function in the absence of realizable information regarding its activity. Even very similar proteins may have every different functions. In the current case, where no specific information is know regarding the function, it is entirely unpredictable what function and activity will be found

for the protein. The prior art does not resolve this ambiguity, since no prior art activity is identified for the encoded polypeptides.

Further, despite knowledge in the art for isolating polynucleotides, the specification fails to provide guidance regarding which amino acids of SEQ ID NO:10 are required to impart a polypeptide as a serine protease. While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity are limited in any protein and the result of such modifications is unpredictable.

The specification, which places weak limitation on the structure of the polypeptides as discussed above, does not support the broad scope of the claims because the specification does **not** establish: (A) regions of the serine protease structure which may be modified without effecting serine protease activity; (B) the general tolerance of to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant

of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for substitutions, deletions, insertions/additions or multiple modifications, as encompassed by the instant claims. Also, the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

Regarding claims 36 and 47, the specification does not teach any therapeutic uses of a pharmaceutical composition or diagnostic markers comprising the polypeptide of the instant invention. Therefore, the specification fails to teach how to use the composition, without undue experimentation, for at least one pharmaceutical use, such as for the prevention, diagnosis, alleviation, treatment, or cure of a disease in the animal to which the substance is administered.

Therefore, one of ordinary skill would require guidance in order to use polypeptides having unknown function and structure and a composition as a therapeutic/diagnostic marker in a manner reasonable correlated with the scope of the claims. Without such guidance, the experimentation left to those skilled in the art is undue.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 36, 41 and 47are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 36, 41 and 47, the phrase "–217th to 240th of SEQ ID NO:10" or "1st to 240th amino acids" are confusing because –217th/240th/1st is the position of the amino acid. For example, the "1st" amino acid of SEQ ID NO:10 is the initial Met residue. These phrases have been interpreted as the amino acid at position –217 of SEQ ID NO:10, for example.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 36, 41 and 47 are rejected under 35 U.S.C. 102(e) as being anticipated by Ruben et al.

Ruben et al. (U.S. Patent Application No. 2004 - form PTO-892) teaches a polypeptide which is 99.8% similar to SEQ ID NO:10 of the instant invention (see SEQ ID NO:108 of Rosen et al.). The polypeptide of Ruben n et al. can be construed as a polypeptide having modifications via substitution, deletion, insertion or addition to SEQ ID NO:10 or fragments of SEQ ID NO:10. Ruben et al. also teaches fragments and variants of said polypeptide ([0020]) and pharmaceutical compositions and diagnostic markers comprising said polypeptides (abstract). Therefore, the teachings of Ruben et al. anticipate claims 36, 41 and 47.

Claim 41 is rejected under 35 U.S.C. 102(b) as being anticipated by Leytus et al.

Leytus et al. (form PTO-892) teaches a polypeptide which be construed as a polypeptide having modifications via substitution, deletion, insertion or addition to SEQ

ID NO:10 or fragments of SEQ ID NO:10. Therefore, the teachings of Leytus et al. anticipate claim 41.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 571-272-0935. The examiner can normally be reached 6:30 A.M. to 5:00 P.M. Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Yong D. Pak
Patent Examiner

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